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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,977	09/05/2006	Kaneo Chiba	B-6121PCT 623711-8	9338

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,977	CHIBA ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *6-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the species of irritation in claim 9 (compression, expansion and vortex flow of the solution by passing the solution through an orifice or perforated plate having a single hole or a lot of holes after receiving the solution in which the microbubbles are suspended) in the reply filed on 4/27/2010 is acknowledged. The traversal is on the ground(s) that while claims 8 and 9 describe different techniques, the common technical features of the techniques should provide overlap in the prior art, and applicant requests that the election requirement be modified to place claims 8 and 9 in effectively the same species as far as prosecution is concerned. This is not found persuasive because claims 8 and 9 include different method steps including "driving a rotor mounted in a vessel" and "passing the solution through an orifice or perforated plate." An examination and search burden for patentably distinct species can require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph. In the instant case, at least different search strategies would be required to address the different method steps. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of

an allowable generic claim as provided by 37 CFR 1.141. The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 1-9 are pending, of which claims 6-8 are withdrawn at this time as being directed to non-elected species. Claims 1-5 and 9 are readable upon the elected species and are examined herein on the merits for patentability.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-13 of

copending Application No. 10/591,979. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of production of nanobubbles by applying physical irritation to abruptly reduce in size microbubbles in solution. Dependent claims in the '979 include that the aqueous solution has electrical conductivity of 300 μs/cm or more. Both sets of claims recite physical irritation caused by compression, expansion and vortex and passing the solution through an orifice having a single opening or a plurality of openings in the dependent claims. Accordingly, the claims are overlapping in scope and are obvious variants of one another. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-5 and 9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-12 of copending Application No. 10/591,978. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of production of nanobubbles by applying physical irritation to abruptly reduce in size microbubbles in a solution having electrical conductivity of 300 μs/cm, including physical irritation caused by compression, expansion and vortex and passing the solution through an orifice having a single opening or a plurality of openings in the dependent claims. Accordingly, the claims are overlapping in scope and are obvious variants of one another. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following reference, drawn to a non-elected species with regard to physical irritation was found during the search for the elected species. It should not be interpreted that a comprehensive search was performed for all non-elected species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 3-5 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Wheatley *et al.* (US 2004/0258760).

Wheatley discloses capsule fabrication of nanobubble surfactant-based ultrasound contrast agents. See Examples 1-2. Span 60 (1.48 g) and NaCl (12.5 g) were crushed with mortar and pestle. Phosphate buffered saline (3 ml) was added to the mixture and crushed to form a paste. An additional 7 ml of PBS was added in a drop-wise fashion to form a suspension. The suspension was then poured into a beaker and rinsed with 10 ml PBS. Tween 80 (1 ml) or Tween-PEG (1 g) was then crushed. A total of 10 ml PBS was added to form a solution. This solution was then added to the suspensions of Span 60 and NaCl, followed by rinsing with 30 ml PBS.

The solution was autoclaved, and sonication of the resulting solution created micro-sized bubbles. The solution was allowed to separate, and the middle layer containing microbubbles was collected into a beaker. The collected microbubbles were then dilued with fresh PBS (1:1 ratio) and mixed to prevent premature separation. The mixture was centrifuged (e.g. a physical irritation) and the bottom layer (nano-bubbles) of solution was collected into 20 ml glass disposable scintillation vials. In example 2, the microbubble solution of Example 1 was transferred to a 50 ml centrifuge and suspended microbubbles were centrifuged for one minute at 500 RPM or 3 minutes at 300 RPM (e.g. a physical irritation). In most cases, the solution separated into two distinct layers: an upper layer containing mostly bubbles and a lower layer containing suspended bubbles in buffer. The liquid (lower) layer of the solution was collected for size and acoustic analysis, and the top layer discarded.

While regard to the limitation of the instant claims that the liquid has an electrical conductivity of 300 μs/cm, it is noted that Wheatley does not specifically recite electrical conductivity. However, the solutions of Wheatley include NaCl and PBS components. Since salts are known in the art to contribute to conductivity of a solution, and since Wheatley performs the same steps as recited in the instant claims to obtain nanobubbles, it is interpreted absent evidence to the contrary that the solutions of Wheatley are inherently capable of achieving the claimed electrical conductivity. Regarding the claimed electrical conductivity, the Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional

characteristics of the claimed product. The propery is descriptive and thus would be an inherent property of the claimed composition. In the absence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable WO 03/022736 in view of JP60-122337, McGrath et al. (US 6,649,145), Bunkin et al. and Aquarius.

The invention is directed to a method of producing a solution comprising nanobubbles having a bubble diameter of 200 nm or less being surrounded by ions at the gas-liquid interface whereby to stabilize the bubbles whereby the method of production includes applying physical irritation to microbubbles contained in a solution having an electrical conductivity of 300 μs/cm to reduce the size of the same.

WO 03/022736 discloses that the merit of water discharge in the product of an oxygenated water is that production and dissolution of the ozone take place at the same time (page 4, lines 10-13). It is disclosed that about 2 liters of an ozonated water with 6 mg/l concentration was produced (page 4, lines 15,16). It is disclosed that fine bubble can be produced by a bubble generator (page 9, lines 13-30). An apparatus is disclosed where the water discharge system has two electrodes insulated with at least one dielectric and an insulator body surrounding the metal electrodes, the water discharge system producing through a dielectric barrier discharge the ozone and ozonated water (Claim 1).

JP 60-122337 disclose the use of a rotation shaft with a screw blade which has thin holes to effect the ozone bubbles (claims, page 3, line 8 to page 4, line 16).

McGrath et al. discloses oxygen nanobubbles having a size of 20-30 nm which are prepared by flowing liquids over hydrophobic surfaces (Column 7, lines 43-55). It is disclosed that nanobubbles allow higher concentrations of oxygen to be achieved in the aqueous solution and that the solutions can be prepared with physiological saline (Column 7, lines 44-65).

Bunkin et al. disclose that submicrobubbles can be stabilized by ions and that these "bubstons" formed in water have a radii of approximately 1-10 nm (Page 208).

Aquarius discloses that a 1000 ppm solution of sodium chloride has an electrical conductivity of 1990 μs/cm (Page 1).

WO 03/022736 disclose the production of ozone bubbles and ozonated water where a dielectric barrier is used to effect the ozone bubbles. The difference between WO 03/0227356 and the claimed invention is that WO 03/022736 does not expressly disclose the use of circulating screwblades which have holes to effect the bubbles or oxygen bubbles that are 200 nm or less, where the water has a salinity concentration corresponding to the claimed electrical conductivity, where the nanobubbles have an inorganic shell of electrolytes, where the electric conductivity of the aqueous solution reaches at least 300μS/cm. However, the prior art amply suggests the same as JP 60-122337 disclose the use of a rotation shaft with a screw blade which has thin holes to effect the ozone bubbles and McGrath discloses that oxygen bubbles having a size of 20-30 nm can be prepared, physiological saline used as the carrier. Bunmkin et al. disclose that submicrobubbles can be stabilized by ions and that these "bubstons" formed in water have a radii of approximately 1-10 nm and Aquarius discloses that a 1000 ppm solution of sodium chloride has an electrical conductivity of 1990 μS/cm. As such, one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation by use of the same that similar to ozone bubbles that oxygen bubbles would exhibit increased dissolution into the water and that the aqueous solution would have a salinity falling within the claimed range of 0.01% to 3.5% via the

use of physiological saline, that the presence of the ions will stabilize the oxygen nanobubbles and that physiological saline will have a electrical conductivity which is greater than 300 μS/cm. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

No claims are allowed at this time.

The following references are made of record as being relevant to the instant invention: US 2004/0118701 and Kim *et al.* (J. Colloid Interface Sci., 2000, 223, p. 285-291).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS